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What is claimed is:

1	1. A	method for predicting single nucleotide polymorphisms, comprising the	
2	steps of:		
3	obtaining	a variation predictiveness matrix; and	
4	predicting	g one or more single nucleotide polymorphisms of a nucleic acid sequence	
5	based on the var	iation predictiveness matrix.	
1	2. T	he method of claim 1 further comprising one or more nucleic acid sequences	
2	with chemical m	odifications.	
1		the method of claim 2, wherein the chemical modifications include	
2	methylation or o	ther chemical groups that incorporate additional charge, polarizability,	
3	hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid		
4	bases or to the n	ucleic acid sequence as a whole.	
1	4. T	The method of claim 1, wherein the step of predicting the likelihood of one or	
1 2		leotide polymorphisms comprises the steps of:	
2			
3	comparing the nucleic acid sequence one or more bases at a time with the variation		
4	predictiveness r	natrix to assign a variation value to bases in the nucleic acid sequence; and	
5	selecting	g the polymorphisms that will likely cause a variation in one or more bases of	
6	the nucleic sequence based on the variation value.		
1	5.	The method of claim 4, wherein the variation in one or more bases is	
2	nonsynonymou		
		The method of claim 4, wherein the variation in one or more bases is	
1		THE HIGHIOU OF Claim 4, whorein the faritation in 2222	
2	synonymous.		
1	7.	The method of claim 1, further comprising the step of generating a dataset of	

single nucleotide polymorphisms for one or more nucleic acid sequences.

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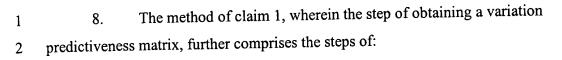
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- calculating a variation frequency from a first base to a second base in a dataset of two

 or more genes; and
- generating the variation predictiveness matrix from the calculated variation frequency.
- 1 9. The method of claim 8 wherein the dataset comprises genes with nucleic acid chemical modifications.
 - 10. The method of claim 9, wherein the chemical modifications include methylation or other chemical groups that incorporate additional charge, polarizability, hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid bases or to the nucleic acid as a whole.
 - 11. The method of claim 8, wherein the variation frequency is determined from a known mutation dataset.
 - 12. The method of claim 8, wherein the variation frequency is determined from a dataset of known diseases.
- 1 13. The method of claim 8, wherein the variation frequency is determined from a dbSNP database.
- 1 14. The method of claim 8, wherein the variation frequency is determined from a non-human mutation database.
- 1 15. The method of claim 8, wherein the variation frequency is determined from a disease-specific database.
- 1 16. The method of claim 8, wherein the variation frequency is determined from a non-human disease database.

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- 1 17. The method of claim 8, wherein the variation frequency is determined from a HGMD database.
- 1 18. The method of claim 8, wherein the variation frequency is determined from a linkage database.
- 1 19. The method of claim 8, wherein the variation frequency is determined from a splice variant database.
- 1 20. The method of claim 8, wherein the variation frequency is determined from a translocation database.
- 1 21. The method of claim 8, wherein the variation frequency is determined from a database of known mutations.
 - 22. The method of claim 8, wherein the variation frequency is further adjusted for wild type genes.
 - 23. The method of claim 8, wherein the variation frequency is further adjusted for engineered or non-naturally occurring genes.
 - 24. The method of claim 8, wherein the variation frequency is further adjusted for conservative polymorphisms.
- 1 25. The method of claim 8, wherein the variation frequency is further adjusted for 2 non-conservative polymorphisms.
- 1 26. The method of claim 8, wherein the variation frequency is further adjusted for 2 cDNA stability.
- 1 27. The method of claim 8, wherein the variation frequency is further adjusted for 2 predicted DNA structure.
- 1 28. The method of claim 8, wherein the variation frequency is further adjusted for 2 predicted RNA structure.

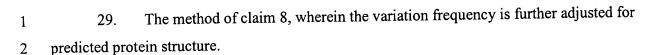
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- 1 30. The method of claim 8, wherein the variation frequency is further adjusted for post-translational modification sequences.
- 1 31. The method of claim 8, wherein the variation frequency is further adjusted for protein stability.
- 1 32. The method of claim 8, wherein the variation frequency is further adjusted for predicted protein transport.
 - 33. The method of claim 8, wherein the variation frequency is further adjusted for shuffled genes.
 - 34. The method of claim 8, wherein the variation frequency is further adjusted for site-directed mutagenesis genes.
 - 35. The method of claim 8, wherein the variation frequency is further adjusted for methylated sequences
 - 36. The method of claim 8, wherein the variation frequency is further adjusted for epigenetic variation.
- The method of claim 8, wherein the nucleic acid sequence comprises a cDNA sequence.
- 1 38. The method of claim 8, wherein the nucleic acid sequence comprises genomic sequence.
- 1 39. The method of claim 8, wherein the nucleic acid sequence comprises an 2 intron/exon boundary.
- 1 40. The method of claim 8, wherein the nucleic acid sequence comprises a transcriptional control sequence.

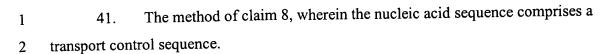
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- 1 42. The method of claim 8, wherein the nucleic acid sequence comprises a translational control sequence.
- 1 43. The method of claim 8, wherein the nucleic acid sequence comprises a transcriptional control sequence.
- 1 44. The method of claim 8, wherein the nucleic acid sequence comprises a splicing control sequence.
 - 45. The method of claim 1, wherein the step of obtaining a variation predictiveness matrix correlates the frequency of a first codon mutation to a second codon mutation with a variation predictiveness value of a nucleic acid sequence from one to ten bases at a time.
 - 46. The method of claim 1, wherein in the variation predictiveness matrix is normalized for the codon usage of a target organism.
 - 47. The method of claim 1, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.
- 1 48. The method of claim 1, wherein the variation predictiveness matrix is 2 generated from a mutant gene dataset that comprises all mutant genes in a mutant gene 3 database minus the known mutant genes of the mutant gene dataset.
- 1 49. The method of claim 1, where the nucleic acid sequence comprises an entire 2 genome.
- 1 50. The method of claim 1, where the nucleic acid sequence comprises a human 2 genome.

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1	51.	The method of claim 1, where the nucleic acid sequence comprises a gene
2	cluster for a t	arget human disease.
1	52.	The method of claim 1, where the variation predictiveness matrix is based
2	a mutant gen	e dataset that comprises a human mutation database.

- The method of claim 1, wherein the steps are affected by a computer program. 53.
- The method of claim 53, wherein the computer program is SNIDE. 54. 1
- The method of claim 53, wherein the computer program is SNooP. 55. 1
- The method of claim 1, wherein the variation predictiveness matrix is 56. 1 determined in silico from a human mutant database. 2
 - The method of claim 1, wherein the step of predicting a likelihood of one or 57. more single nucleotide polymorphisms is determined in silico.
 - A method for creating a variation predictiveness value for use in a variation 58. predictiveness matrix, comprising the steps of:
 - calculating the variation frequency from a first nucleic acid to a second nucleic acid in a dataset of two or more variations; and
- determining a variation predictiveness value from the calculated variation frequency. 5
- The method of claim 58, further comprising the step of generating a variation 59. 1 predictiveness matrix that correlates the frequency of a first to a second variation with the 2 variation predictiveness value. 3
- The method of claim 58, wherein the dataset comprises genes with nucleic 60. 1 acid chemical modifications. 2
- The method of claim 60, wherein the chemical modifications include 61. 1 methylation or other chemical groups that incorporate additional charge, polarizability, 2

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- 3 hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid
- 4 bases or to the nucleic acid as a whole.
- 1 62. The method of claim 58, wherein the variation frequency is determined from a known mutation dataset.
- 1 63. The method of claim 58, wherein the variation frequency is determined from a dataset of known diseases.
- 1 64. The method of claim 58, wherein the variation frequency is determined from a 2 dbSNP database.
- 1 65. The method of claim 58, wherein the variation frequency is determined from a non-human mutation database.
 - 66. The method of claim 58, wherein the variation frequency is determined from a disease-specific database.
 - 67. The method of claim 58, wherein the variation frequency is determined from a non-human disease database.
- 1 68. The method of claim 58, wherein the variation frequency is determined from a 2 HGMD database.
- 1 69. The method of claim 58, wherein the variation frequency is determined from a linkage database.
- 1 70. The method of claim 58, wherein the variation frequency is determined from a splice variant database.
- 1 71. The method of claim 58, wherein the variation frequency is determined from a translocation database.
- The method of claim 58, wherein the variation frequency is determined from a database of known mutations.

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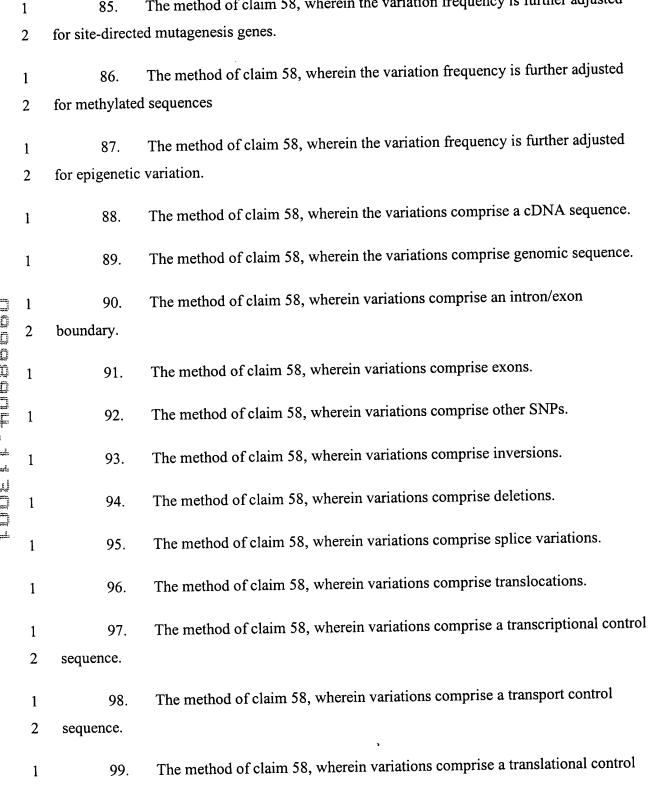
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- The method of claim 58, wherein the variation frequency is further adjusted 73. 1 2 for wild type genes.
- The method of claim 58, wherein the variation frequency is further adjusted 74. 1 for engineered or non-naturally occurring genes. 2
- The method of claim 58, wherein the variation frequency is further adjusted 75. 1 for conservative polymorphisms. 2
- The method of claim 58, wherein the variation frequency is further adjusted 76. 1 for non-conservative polymorphisms. 2
- The method of claim 58, wherein the variation frequency is further adjusted 77. 1 2 for cDNA stability.
 - The method of claim 58, wherein the variation frequency is further adjusted 78. for predicted DNA structure.
 - The method of claim 58, wherein the variation frequency is further adjusted 79. for predicted RNA structure.
- The method of claim 58, wherein the variation frequency is further adjusted 80. for predicted protein structure. 2
- The method of claim 58, wherein the variation frequency is further adjusted 81. 1 for post-translational modification sequences. 2
- The method of claim 58, wherein the variation frequency is further adjusted 82. 1 for protein stability. 2
- The method of claim 58, wherein the variation frequency is further adjusted 83. 1 2 for predicted protein transport.
- The method of claim 58, wherein the variation frequency is further adjusted 84. 1 2 for shuffled genes.

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sequence.



The method of claim 58, wherein the variation frequency is further adjusted

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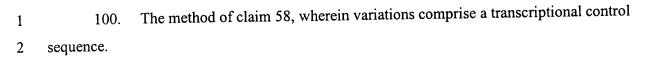
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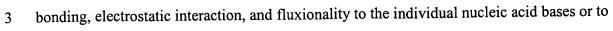
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- 1 101. The method of claim 58, wherein variations comprise a splicing control sequence.
- 1 102. The method of claim 59, wherein in the variation predictiveness matrix is 2 normalized for the nucleotide usage of a target organism.
 - 103. The method of claim 59, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.
 - 104. The method of claim 58, wherein the variation predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.
 - 105. The method of claim 58, where the nucleic acid comprises one or more bases.
 - 106. The method of claim 58, where the nucleic acid comprises DNA.
 - 107. The method of claim 58, where the nucleic acid comprises RNA.
- 1 108. The method of claim 58, where the nucleic acid comprises a triplet.
- 1 109. The method of claim 58, The method of claim 16, where the nucleic acid comprises a codon.
- 1 110. The method of claim 58, The method of claim 16, where the nucleic acid comprises one or more non-sequence base modifications.
- 1 The method of claim 58, where the nucleic acid comprises modified nucleic 2 acids.
- 1 112. The method of claim 58, wherein modified nucleic acids include methylation 2 or other chemical groups that incorporate additional charge, polarizability, hydrogen



- 4 the nucleic acid as a whole.
- 1 113. The method of claim 58, where the nucleic acid comprises an entire genome.
- 1 114. The method of claim 58, where the nucleic acid comprises a human genome.
- 1 115. The method of claim 58, where the nucleic acid comprises a gene cluster for a target human disease.
- 1 116. The method of claim 58, where the variation predictiveness matrix is based on 2 a mutant gene dataset that comprises a human mutation database.
- 1 117. The method of claim 58, wherein the steps are affected by a computer 2 program.
- 1 118. The method of claim 58, wherein the computer program is SNIDE.
- 1 119. The method of claim 58, wherein the computer program is SNooP.
 - 120. The method of claim 58, wherein the variation predictiveness value is determined in silico from a human mutant database.
- 1 121. The method of claim 58, wherein the step of predicting a likelihood of one or 2 more single nucleotide variation is determined in silico.
- 1 122. A method for creating a polymorphism predictiveness value for use in a 2 mutation predictiveness matrix, comprising the steps of:
- calculating the mutation frequency from a first codon to a second codon in a dataset

 of two or more mutant genes; and
- determining a polymorphism predictiveness value from the calculated mutation frequency.

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123.	The method of claim 122, further comprising the step of generating a codon
polymorphism	n predictiveness matrix that correlates the frequency of a first to a second codor
mutation with	the polymorphism predictiveness value.

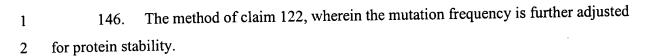
- 1 124 The method of claim 122, wherein the dataset comprises nucleic acids with chemical modifications.
- 1 125 The method of claim 124, wherein the chemical modifications include 2 methylation or other chemical groups that incorporate additional charge, polarizability, 3 hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid 4 bases or to the nucleic acid as a whole.
 - The method of claim 122, wherein the mutation frequency is determined from a known mutation dataset.
 - The method of claim 122, wherein the mutation frequency is determined from a dataset of known diseases.
 - The method of claim 122, wherein the mutation frequency is determined from a dbSNP database.
 - The method of claim 122, wherein the mutation frequency is determined from a non-human mutation database.
- 1 130 The method of claim 122, wherein the mutation frequency is determined from 2 a disease-specific database.
- 1 131 The method of claim 122, wherein the mutation frequency is determined from 2 a non-human disease database.
- 1 132. The method of claim 122, wherein the mutation frequency is determined from 2 a HGMD database.
- 1 133. The method of claim 122, wherein the mutation frequency is determined from 2 a linkage database.

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- 1 134. The method of claim 122, wherein the mutation frequency is determined from 2 a splice variant database.
- 1 135. The method of claim 122, wherein the mutation frequency is determined from 2 a translocation database.
- 1 136. The method of claim 122, wherein the mutation frequency is determined from 2 a database of known mutations.
- 1 137. The method of claim 122, wherein the mutation frequency is further adjusted 2 for wild type genes.
- 1 138. The method of claim 122, wherein the mutation frequency is further adjusted 2 for engineered or non-naturally occurring genes.
 - 139. The method of claim 122, wherein the mutation frequency is further adjusted for conservative polymorphisms.
 - 140. The method of claim 122, wherein the mutation frequency is further adjusted for non-conservative polymorphisms.
- 1 141. The method of claim 122, wherein the mutation frequency is further adjusted 2 for cDNA stability.
- 1 142. The method of claim 122, wherein the mutation frequency is further adjusted 2 for predicted DNA structure.
- 1 143. The method of claim 122, wherein the mutation frequency is further adjusted 2 for predicted RNA structure.
- 1 144. The method of claim 122, wherein the mutation frequency is further adjusted 2 for predicted protein structure.
- 1 145. The method of claim 122, wherein the mutation frequency is further adjusted 2 for post-translational modification sequences.

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- 1 147. The method of claim 122, wherein the mutation frequency is further adjusted for predicted protein transport.
- 1 148. The method of claim 122, wherein the mutation frequency is further adjusted 2 for shuffled genes.
- 1 149. The method of claim 122, wherein the mutation frequency is further adjusted 2 for site-directed mutagenesis genes.
- 1 150. The method of claim 122, wherein the mutation frequency is further adjusted 2 for methylated sequences
 - 151. The method of claim 122, wherein the mutation frequency is further adjusted for epigenetic variation.
 - 152. The method of claim 122, wherein the mutant genes comprise a cDNA sequence.
- 1 153. The method of claim 122, wherein the mutant genes comprise genomic 2 sequence.
- 1 154. The method of claim 122, wherein mutant genes comprise an intron/exon 2 boundary.
- 1 155. The method of claim 122, wherein mutant genes comprise exons.
- 1 156. The method of claim 122, wherein mutant genes comprise other SNPs.
- 1 157. The method of claim 122, wherein mutant genes comprise inversions.
- 1 158. The method of claim 122, wherein mutant genes comprise deletions.
- 1 159. The method of claim 122, wherein mutant genes comprise splice variations.

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- 1 160. The method of claim 122, wherein mutant genes comprise translocations.
- 1 161. The method of claim 122, wherein mutant genes comprise a transcriptional control sequence.
- 1 162. The method of claim 122, wherein mutant genes comprise a transport control 2 sequence.
- 1 163. The method of claim 122, wherein mutant genes comprise a translational control sequence.
- 1 164. The method of claim 122, wherein mutant genes comprise a transcriptional control sequence.
 - 165. The method of claim 122, wherein mutant genes comprise a splicing control sequence.
 - 166. The method of claim 123, wherein in the codon polymorphism predictiveness matrix is normalized for the codon usage of a target organism.
 - 167. The method of claim 123, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database.
- 1 168. The method of claim 123, wherein the codon polymorphism predictiveness 2 matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant 3 gene database minus the known mutant genes of the mutant gene dataset.
- 1 169. The method of claim 122, where the codon comprises one or more bases.
- 1 170. The method of claim 122, where the codon comprises DNA.
- 1 The method of claim 122, where the codon comprises RNA.
- 1 The method of claim 122, where the codon comprises a triplet.
- 1 173. The method of claim 122, where the codon comprises a codon.

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1	174.	The method of claim 122, where the codon comprises one or more non-
2	sequence base	e modifications.
1	175.	The method of claim 122, wherein the codon further comprises modifications.
1	176.	The method of claim 122, wherein modifications include methylation or other
2		ups that incorporate additional charge, polarizability, hydrogen bonding,
3	electrostatic i	nteraction, and fluxionality to the individual nucleic acid bases or to the nucleic
4	acid as a who	le.
1	177.	The method of claim 122, where the codon comprises an entire genome.
1	178.	The method of claim 122, where the codon comprises a human genome.
1	179.	The method of claim 122, where the codon comprises a gene cluster for a
2	target human	disease.
1	180.	The method of claim 122, where the codon polymorphism predictiveness
2	matrix is bas	ed on a mutant gene dataset that comprises a human mutation database.
1	181.	The method of claim 122, wherein the step of predicting a likelihood of one or
2	more single	nucleotide polymorphisms is determined in silico.
1	182.	A method for creating a variation predictiveness matrix, comprising the steps
2	of:	
3	calcu	lating the variation frequency from a first nucleic acid to a second nucleic acid
4	in a dataset	of two or more variations;
5		mining a variation predictiveness value from the calculated variation frequency;
6	and	

a second nucleic acid with the variation predictiveness value.

generating a variation predictiveness matrix that correlates the frequency of a first to

1	183. The method of claim 182, wherein the dataset comprises nucleic acids wi	ih	
2	chemical modifications.		
1	184. The method of claim 183, wherein the chemical modifications include		
2	methylation or other chemical groups that incorporate additional charge, polarizability,	d	
3	hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid	u	
4	bases or to the nucleic acid as a whole.		
1	185. The method of claim 182, wherein the variation frequency is determined	from	
2	a variation dataset.		
1	186. A method for creating a polymorphism predictiveness matrix, comprising	g the	
2	steps of:		
3	calculating the mutation frequency from a first codon to a second codon in a data	iset	
4	of two or more mutant genes;		
5	determining a polymorphism predictiveness value from the calculated mutation		
6	frequency; and		
	and the free state of the free		
7	generating a codon polymorphism predictiveness matrix that correlates the frequency		
8	of a first to a second codon mutation with the polymorphism predictiveness value.		
1	187. The method of claim 186, wherein the dataset comprises nucleic acids w	ith	
2	chemical modifications.		
1	188. The method of claim 187, wherein the chemical modifications include		
2	methylation or other chemical groups that incorporate additional charge, polarizability,		
3	hydrogen bonding, electrostatic interaction, and fluxionality to the individual nucleic acid		
4	bases or to the nucleic acid as a whole.		
1	189. The method of claim 186, wherein in the codon polymorphism predictive	eness	
2.	matrix is normalized for the codon usage of a target organism.		

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190.	The method of claim 186, wherein the codon polymorphism predictiveness	
matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutan		
gene datahase.		

- 191. The method of claim 186, wherein the codon polymorphism predictiveness matrix is generated from a mutant gene dataset that comprises all mutant genes in a mutant gene database minus the known mutant genes of the mutant gene dataset.
- 1 192. The method of claim 186, wherein the codon comprises one or more bases.
- 1 193. The method of claim 186, where the codon comprises a triplet.
- 1 194. The method of claim 186, where the codon comprises a codon.
- 1 195. The method of claim 186, where the codon comprises one or more nonsequence base modifications.
 - 196. An isolated and purified nucleic acid comprising a predicted single nucleotide variation of a nucleic acid sequence based on the variation predictiveness matrix sequence of claim 1.
 - 197. An isolated and purified nucleic acid comprising a predicted single nucleotide polymorphism of a wild-type gene sequence based on the codon mutation predictiveness matrix sequence of claim 1.
 - 198. An apparatus for detecting a single nucleotide polymorphism comprising:
- 2 a substrate; and
- one or more isolated and purified nucleic acids comprising a predicted single
 nucleotide variation of a nucleic acid sequence based on a variation predictiveness matrix
 sequence affixed to the substrate.
- 1 199. The apparatus of claim 198, wherein the substrate comprises a
 2 microfabricated solid surface to which molecules may be attached through either covalent or
 3 non-covalent bonds.

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Attorney Docket No. 19929-1037		
_	The apparatus of claim 198, wherein the substrate further comprises adgett films, glass, functionalized glass, germanium, silicon, PTFE, polystyres aide, gold, silver, or any materials comprising amino, carboxyl, thiol or hydroxyl	
functional groups incorporated on a planar or spherical surface.		
201.	An apparatus for detecting a single nucleotide polymorphism comprising:	

- 2 a substrate; and
- one or more isolated and purified nucleic acids comprising a predicted single
 nucleotide polymorphism of a wild-type gene sequence based on a codon polymorphism
 predictiveness matrix. sequence affixed to the substrate.
 - 202. The apparatus of claim 201, wherein the substrate comprises a microfabricated solid surface to which molecules may be attached through either covalent or non-covalent bonds.
 - 203. A computer program embodied on a computer readable medium for predicting variations, comprising:
 - a code segment for creating variation predictiveness matrix from a nucleic acid dataset;
- a code segment for comparing a wild-type gene sequence with the variation predictiveness matrix; and
- a code segment for predicting variations in the wild-type gene sequence based on the comparison.
- 204. A computer program embodied on a computer readable medium for predicting polymorphisms, comprising:
- a code segment for creating a codon mutation predictiveness matrix from a mutant gene dataset;

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	5	a code segment for comparing a wild-type gene sequence with the codon
	6	polymorphism predictiveness matrix; and
	7	a code segment for predicting polymorphisms in the wild-type gene sequence based
	8	on the comparison.
	1	205. A polymorphism prediction dataset, comprising:
	2	a first nucleic acid;
	3	a second nucleic acid variation that correlates to a polymorphism from the first
	4	nucleic acid; and
	5	a variation predictiveness value determined from known variations in a variation
T J	6	database for a target organism.
	1	206. A polymorphism prediction dataset, comprising:
	2	a first codon;
	3	a second codon mutation that correlates to a mutation from the first codon; and
	4	a codon polymorphism predictiveness value determined from known mutations in a
	5	mutation database for a target organism.
	1	207. A single nucleotide polymorphism determined by the method of claim 1.
	1	208. A method for predicting single nucleotide polymorphisms, comprising the
	2	steps of:
	3	inputing each codon in a queried nucleic acid sequence;
	4	determining each possible nonsynonymous mutation;
	5	assigning a predictiveness value to that mutation based on the identity of the wild-
	6	tune and resultant codon; and





7	ranking	g of all predictiveness values to highlight the likely to occur and impact gene
8	function.	
1	209.	The method of claim 208, further comprising the steps of:
2	parsing	g one or more nucleic acid sequence input files having sequence information;
3	calcula	ting an expected mutation liklihood according to a user-defined threshold; and
4	ranking	g of point mutation predictions by a ζ -value.
1	210.	The method of claim 208, further comprising the step of generating a
2	delimited file	suitable for a standard spreadsheet application.
1	211.	An isolated and purified nucleic acid comprising SEQ ID NOS.: 1-12.
1	212.	An isolated and purified nucleic acid comprising a cardiomyopathy disease
2	related SNP selected from the group consisting essentially of BDKRB2, EDNRA, ADRB1,	
3	ADRB2, CRE	B1 and MCIP.
1	213.	An isolated and purified nucleic acid of claim 211, wherein the SNP is Thr-
2	>Met substitu	ation in BDKRB2 at position 383.